Genetic Databases

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WORLD HEALTH ORGANIZATION - ORGANISATION MONDIALE DE LA SANTE

GENETIC DATABASES

ASSESSING THE BENEFITS AND THE IMPACT ON HUMAN & PATIENT RIGHTS

European Partnership on Patients' Rights and Citizens' Empowerment
A network of the World Health Organisation Regional Office for Europe

Contents

Preface: Setting the Scene

Advances in all fields of technology have contributed significantly to the threat that individuals feel to their personal interests in contemporary society. This is particularly true of the degree of concern that individuals harbour about their personal privacy. This concern is felt most acutely in the realm where technologies converge, and recent and rapid advances in the development of computer and genetic technologies pose one of the most significant challenges to the protection of individual interests in recent years.

As more becomes known about the human genome and the influence of genes on our lives, so advances in computer technology mean that this information can be stored, analysed, disseminated and applied with accuracy and efficiency as never before. And, while it is undeniable that the generation of this knowledge brings enormous potential to benefit humanity, it is also self-evident that this new knowledge carries an attendant risk of harm to the individuals to whom it relates and their families, as well as of prejudice to the human rights of entire communities. In the context of many forms of genetic information, this potential for harm arise not only for the individuals who have provided the information, but also for the blood relatives of such persons. This is because of the essential nature of most genetic conditions; they are passed from one generation to the next. Thus, those who share a common genetic heritage also share a common interest in how their genetic information is used.

By corollary, genetic information can be extremely useful to parties outside the family unit, such as employers, insurers, the state, and researchers. In this latter respect, the creation of genetic databases holds enormous promise in research terms. These databases might hold the key to a better understanding of genetic disease, and, perhaps one day, cures and therapies may be found for conditions for which little can be done at the present time.

We have, then, a fundamental tension between the possibility of considerable public good on the one hand, and the potential for significant individual and familial harm on the other. The basic interests that lie in the balance are those between human dignity and human rights as against public health, scientific progress and commercial interests in a free market.

This report examines the ethical, social and legal issues that surround the creation and operation of databases containing human genetic material. In light of the considerable complexities which beleaguer this area, the report contains proposed international guidelines to govern the establishment, uses, and maintenance of these databases, and access thereto. It is important to note, however, that genetic influences rarely determine an individual's health status, and they never determine what it means to be an individual. And, while genetic factors might play a part in many diseases, often their influence is no greater than that of other factors, such as environment or life-style. It is, therefore, of crucial importance that we do not place too much emphasis on genetics in discussing 'the human condition'. We are, each of us, more than the sum of our genetic component parts.

The report has been prepared under the auspices of the WHO's European Partnership on Patients' Rights and Citizens' Empowerment.

Working Group Membership

This report has been prepared by a Working Group consisting of:

Fons Dekkers
Vice-President
European Public Health Alliance
Driebergen, The Netherlands

Alastair Kent
Director
Genetics Interest Group
London, England

Graeme Laurie (Convener)
Faculty of Law
University of Edinburgh
Edinburgh, Scotland

Carmel Shalev
Director
Unit for Health Rights and Ethics
Gertner Institute for Health Policy Research
Hashomer, Israel

1. Introduction

1.1 What is genetic information ?

A crucial starting point in any discussion of genetic information is the realisation that this is not a unified concept. The World Health Organisation is primarily interested in health-relevant information. Nonetheless, even within this category many different forms of genetic information exist. For example, it becomes increasingly clear as more work is done on the Human Genome Project (HGP) and other genetic research projects, that many, if not most, diseases have a genetic component. Thus, information about such diseases might be termed 'genetic information'. More broadly still, it is arguable that information about one's skin colour or sex is, in fact, genetic information. Indeed, even family history is a very important source of genetic information, albeit subject to the vagaries of failing memories or misunderstood conditions. Such a broad view, however, makes genetic information indistinguishable from general health information.

More specific forms of genetic information include the results of DNA analysis, such as genetic tests for monogenic recessive or dominant conditions, where degrees of risk are high and predictions of inheritance are relatively straight-forward. Less specific forms of information that can be derived from testing include susceptibility data, which, while remaining genetic information, reveal nothing more significant or determinative in the causal mechanism of disease than the role of other factors, such as the environment or the interaction of a number of genes.

Accordingly, there are gradations of information that might be termed genetic, and it is not proposed that an unifying definition be offered here. Indeed, a starting premise must be that the term 'genetic information' is a false construct. None the less, in normative terms, it is at least possible to identify factors that are relevant in influencing whether information is classed as genetic. These might be termed *event size criteria*, i.e. - criteria by reference to the significance of which, information is judged to be genetic. The significance of these criteria in rendering information genetic might be actual or perceived. For example, scientifically verifiable data which are derived from direct analysis of the DNA molecule can clearly be defined as genetic, whether or not they reveal anything of clinical significance for the individual concerned. In contrast, a perceived influence of genes on a condition might imbue information about the condition with genetic significance in the minds of many, even if the reality is that other, possible stronger, factors are operative in the onset of disease.

While it is important to recognise that a discussion of genetic information is necessarily more wide-ranging than the narrow context of genetic databases, the focus of this report is the latter topic, and so the former is examined accordingly. But, because we cannot easily distinguish between genetic information and medical information more generally, it is important also to set this discussion of genetic databases in the wider context of health databases. However, this is not to deny that certain elements of certain forms of genetic information throw up particular problems. A clear example of this are monogenic disorders and the impact that information about them can have on families affect by them. This is because of the relatively high predictability of disease in relatives which accompanies such disorders. Thus, in many ways, knowledge of one's own status is also knowledge about the possible health status of a relative. In such circumstances, the argument can be put that the information belongs to the family and not simply to the individual who has been tested. If this is accepted, however, it raises the problem

of how to resolve conflicts over use or non-use of the information, and it also raises the question of who should speak for 'the family'.

It is axiomatic, then, that the contents of this report are also likely to have direct and significant impact on any database that contains personal health information. The starting premise is that the accepted principles regarding personal health information and human rights apply also to genetic information.

1.2 What is a database ?

In this report a 'database' shall be taken to include any methodical or systematic collection of data, structured in a fashion that allows accessibility to individual or collective elements of that database by electronic, manual or any other means.

2. A Human Rights Framework

2.1 Existing protections

This report is set against a background of existing international measures designed to protect human and patients' rights. These measures are embodied in a number of instruments, including the following:

- United Nations Universal Declaration on Human Rights (1948)
- European Convention on Human Rights (1950)
- The Convention on the Elimination of All Forms of Racial Discrimination (1965)
- Article 15 of the International Covenant on Economic, Social and Cultural Rights (1966)
- The Convention on the Elimination of All Forms of Discrimination Against Women (1979)
- International data protection measures, including the Council of Europe's Convention for the Protection of Individuals with Regard to Automatic Processing of Personal Data (28 January 1981, ETS No. 108); the Council of Europe's Recommendation on regulations for automated medical databanks (No. R (81) 1), and the EC Directive on the Protection of Individuals with Regard to the Processing of Personal Data and on the Free Movement of Such Data (95/46/EC)
- CIOMS, International Guidelines for Ethical Review of Epidemiological Studies (1991)
- Bio-diversity Convention (1992)
- CIOMS, International Ethical Guidelines for Biomedical Research Involving Human Subjects (1993)
- WHO Declaration on the Promotion of Patients' Rights (1994)
- UNESCO Universal Declaration on the Human Genome and Human Rights (1997)
- Council of Europe Recommendation on the Protection of Medical Data (1997, No. R (97)5)
- WHO International Guidelines on Ethical Issues in Medical Genetics and Genetic Services (1997)
- Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, (1997)
- World Health Assembly statement on "Cloning in Human Reproduction" (WHO 50.37)
- Council of Europe Protocol on Cloning (1998)
- The Helsinki Declaration (Recommendations Guiding Physicians in Biomedical Research involving Human Subjects, revised 2000)

2.2 Fundamental guiding values

It is possible to derive from these instruments a set of common values that both underpin these measures and provide a justification for them. Moreover, these values can be offered as a hierarchy of fundamentals which inform and guide human interaction and the treatment of human beings. These are:

- The pursuit of human well-being
- The quality of human dignity, including fundamental human rights and the principle of non-discrimination
- The principle of respect for persons, including the imperatives of beneficence and non-maleficence
- The principle of respect for individual autonomy

Various means exist by which these values are embodied in social and legal norms. Two important examples are those of respect for individual privacy, and the recognition of the individual interest in controlling certain intimate adjuncts to one's personality, such as the use and dissemination of personal information.

These values, and the means to protect them, equally underpin this report. They inform the debate that is contained herein, and they govern the formulation of the recommendations that are offered.

2.3 Establishing parameters and re-evaluating human rights paradigms

Several caveats must be noted. First, the international instruments cited above are concerned primarily with the protection of the individual. As a starting point, therefore, the focus of this report is human rights and their protection, and the ways in which these rights are threatened by the generation of genetic information and its storage in data banks and databases. However, it will be necessary to depart in certain cases from a strictly individualistic and atomistic approach, for it is an important feature of certain forms of genetic data that they also reveal information about the blood relatives of the person from whom the data were originally derived, as well as their ethnic communities. In this respect, an individualistic, autonomy-driven perspective does not assist in the resolution of the various claims or conflicts which might arise surrounding this information and its use.

Second, a common measure seen in these international instruments, as a counter-balance to individual rights, is the public interest in the advancement of scientific knowledge and the promotion of public health. It is frequently on this ground that (genetic) databases are justified by the state and commercial bodies. More broadly, it is an appeal that it is often made to override individual rights or to reduce the protection afforded to them. Accordingly, the role of the public interest requires close scrutiny in tandem with any examination of individual rights. No individual rights are absolute. Inevitably, therefore, a balance of legitimate interests is required.

The value of databases derives from the collective nature of their data. Often, the prospect of direct individual benefit is minimal. Thus, the justification for a database is more likely to be grounded in communal value, and less on individual gain. And, while this is not to say that individual protection should be ignored, it leads to the question whether the individual can remain of paramount importance in this context. Although protections can and should be instituted for individuals who surrender personal data, the achievement of optimal advances in

the name of the collective good may require a reconsideration of the respective claims so as to achieve an appropriate balance between individual and collective interests, including those of ethnic minorities, from a multi-cultural perspective.

This report endorses the universalisability of human rights, and it is considered that its recommendations equally enjoy this quality. However, it is recognised that the views expressed in this report might be deemed to be uniquely western in nature, and it is recommended that the World Health Organisation consider further investigation of the issues raised from a non-Western perspective.

Recommendation 1: The World Health Organisation should investigate the issues raised by genetic databases from perspectives other than that which reflects a western, Judeo-Christian ethic.

3. General Principles

3.1 The nature of individual claims

It is important to distinguish between (a) physical samples taken from individuals, such as a blood or saliva sample, and, (b) genetic information derived from these samples. While any claim made to a physical sample can only legitimately come from the sample source, the same is not true of genetic knowledge that arises from of the sample, for this might have consequences for a wider circle of persons, such as blood relatives.

Body samples, and information derived from them, represent two of the most intimate aspects of ourselves. Accordingly, we have a very strong claim to control these elements and their uses. Indeed, in ethical terms, that claim is akin to a property right, in that the primary control should always remain with the individuals who can stake a claim to samples or the information generated from them. It should be irrelevant where, or how, these elements are gathered or stored. The primary point of reference should be the individual or the family, unless the intimate connection between the persons and the samples or the information has been lost, for example, through anonymisation. Where that relationship remains, the inalienable nature of the individual's claim should be reflected in the fact that she cannot give away her personal information. At best, this information can be *shared* with third parties, for example with family members to further their own health interests, or with researchers, employers and insurers who should be deemed only to received such information in a custodial capacity.

This is not to say, however, that there should be no limits to this right of control. While no individual can be forced to provide a sample or information, in certain circumstances the exercise of control over samples and information can be legitimately curtailed, if, for example, this will result in unwarranted harm to others. Thus, certain uses of genetic information that might impact on family members can be prohibited, and gifting of samples or information should never be made subject to qualification or restriction.

It is also apposite to consider the legitimacy of obtaining and using genetic samples and data derived from them for the purposes of criminal investigation and prosecution. While a clear public interest can be furthered in this regard, it remains subject to the need for stringent safeguards of individual liberties and human rights. A consideration of such a model in detail is

beyond the scope of this report, whose focus is genetic data obtained and used for research and health purposes.

Recommendation 2: The intimate and unique relationship that individuals have with body samples or information derived from them deserves full recognition and proper respect. Individuals are entitled to control over the use of their samples and information, in a manner akin to a property right. This right may, however, be subject to waiver or certain limits, such as when anonymisation occurs (and so the relationship is lost), or when certain uses may cause harm to others.

3.2 The obligations we owe concerning our genetic information

The generation of genetic information gives rise to both rights and responsibilities. There can be much value in genetic information beyond that which it represents to the individual to whom it relates. A number of other parties can actively benefit from access to genetic information, or this can avert harm to them. In particular, several public interests can be furthered by the judicious use of such information. For example, the investigation and prosecution of crimes can be greatly assisted by the existence of forensic databases; public health measures can be better implemented with access to relevant epidemiological data, and a host of research ends can be advanced through the establishment of genetic databases. In addition, a range of strong familial interests can be protected, and significant harm can be averted in some cases. For all of these reasons, a ethical case can be made that we each have a moral imperative to share our genetic information if some, or any, of these ends can be furthered. Thus duties might be owed to (i) the community, (ii) certain institutions acting in the public interest, or (iii) one's own family. The strength of the imperative grows as we move closer to the family unit.

This is in no way to suggest that individuals should be forced to share their genetic information. Rather, it is to stress the need for a balance of interests. This is the most ethically justifiable approach to the management of genetic information. Moreover, it acknowledges that in certain circumstances the balance of interests might weigh more heavily towards public interests and away from more traditional ways of respecting individual rights. For example, access to archived genetic material can further a number of important research ends that might hold considerable promise of public benefit, but it might prove impossible to obtain informed consent from the sample sources. Should we depart in such cases from the requirement of informed consent? This is discussed below, but it is important to note that a strong case can be made that the balance of interests here should be tipped in favour of the public interest, subject always to protection of privacy, except where the health of a particular identifiable individual is at stake. However, in all circumstances, a suitable and rigorous process of weighing and balancing of interests must be undertaken to ensure adequate respect and protection for individuals. This is an imperative from which no departure is permissible.

3.3 The legitimate establishment of genetic databases

This report endorses the Council of Europe recommendations that genetic data collected and processed for preventive treatment, diagnosis or treatment of the data subject or for scientific research should only be used for these purposes or to allow the data subject to take free and informed decision on these matters. Outside these purposes, the collection and processing of genetic data should, in principle, only be permitted for health reasons and in particular to avoid any serious prejudice to the health of the data subject or third parties. However, the collection and processing of genetic data in order to predict illness may be allowed for in cases of

overriding interest and subject to appropriate safeguards defined by law (Council of Europe Recommendation on the Protection of Medical Data (1997, No. R (97)5, paras. 4.7 and 4.9).

In the context of the creation of databases, there are therefore a number of legitimate health-related purposes for which genetic data can be collected, processed, stored and analysed. These might be presented as (a) pure research uses, (b) clinical research uses and development of pharmaceutical or other therapeutic products, (c) uses leading to direct benefit to patients or their families. The relationship of the parties is different in each of these scenarios. It is important to understand the nature of each relationship, for this will dictate in larger measure the respective rights and duties of the parties. In (a), the relationship is that of researcher and research subject, and the respective obligations and entitlements are defined accordingly. In (c), the primary relationship is that of health care professional and patient. This is a therapeutic alliance, where the rights and duties are stronger than in (a), and the primary obligations of the health care professional are to do good for, and no harm to, her patient. Finally, in (b), the relationship is a hybrid of (a) and (c), in that the health care professional acts both as clinician and researcher. It is in this context that most potential for conflict arises. Often, however, it is difficult to establish an absolute distinction between clinical and research uses of information. Clinical investigation, particularly in the context of rare disorders, can easily tip into the realm of research. In such circumstances, the professionals involved should be mindful of their dual responsibilities as clinician and researcher alike, but beyond this it is not advisable for this report to offer concrete guidance, other than to stress the important of informed-consent principles in regulating clinical relationships. Any exception to, or deviation from, these principles arising from specific research responsibilities of clinicians should be communicated clearly to the patient concerned. If there is a conflict of interests or a lack of consent, ethical standards and professional responsibilities derived from the clinical relationship with the patient should always prevail.

At all times, there must be adequate safeguards to ensure that those who would establish, maintain or gain access to a database are responsible, competent and professional with respect to their duties, requests or uses concerning the database and its contents.

Recommendation 3: The collection of genetic data should be only be allowed, in the first instance, for the purpose of promoting public health. The onus is on those who would seek to use data outside this purposes to justify doing so.

Whatever the reasons for the establishment of a genetic database, the onus will be on those who seek to create the database to justify its nature, purposes, content and uses. In particular the following factors must be satisfactorily established:

(1) The public interest that will be furthered by the creation of the database;
(2) The relevance of genetic data to the purposes of the database;
(3) That the creators of the database are able to restrict the use of the data to the purposes for which it was sought;
(4) That the creators of the database are able to ensure adequate security measures for the data and for privacy protection;
(5) That the creators and users of the database have sufficient competence to understand the data;
(6) That the creators and users of the database have the ability to understand the context in which the information comes, and the relevance of other factors which further contextualise the information.

(7) That the creators have considered ethical aspects and made appropriate provisions to respect human rights.

3.4 The need for ethical reflection and scrutiny

The decision to create a genetic database is an ethically significant act. This is also true of the decision not to create such a database. Neither option is ethically neutral. But, once the decision has been taken to establish a database, this must be justified in ethical terms.

Recommendation 4: It is recommended that an appropriate ethical approval mechanisms be established to oversee the creation and maintenance of genetic databases. An appropriate means to do so would be to establish an Ethical Approval Committee with the following duties:

(1) To ensure minimal standards and public trust in the database;
(2) To scrutinize the scientific validity of any proposal to establish a database;
(3) To ensure the reputation and integrity of the creators of the database;
(4) To verify that an identified public interest can be furthered by the establishment of the database;
(5) To assess and review the adequacy of security provisions of the data held on the database for the protection of privacy;
(6) To assess and review any other proposed protection mechanisms in respect of the persons to whom the data relate;
(7) To consider and address ethical questions concerning the use of the database, and the data contained therein;
(8) To produce Codes of Conduct governing the establishment and maintenance of genetic databases.

It should be borne in mind that such an ethical body would require to reflect the particular context in which genetic data were being generated and used. In particular, the composition of the body, and its focus, will be different depending on whether the genetic data exist in the context of (a) pure research, (b) clinical research, or (c) clinical practice.

3.5 The need for public debate

Article 28 of the Council of Europe *Convention on Human Rights and Biomedicine* provides: 'Parties to this Convention shall see to it that the fundamental questions raised by the developments of biology and medicine are the subject of appropriate public discussion in the light, in particular, of relevant medical, social, economic, ethical and legal implications, and that their possible application is made the subject of appropriate consultation.'

It is imperative that public debate precede the establishment of new genetic databases, in light of the considerable implications that their existence can have for a wide range of parties, and the public interest more generally.

Moreover, crucial to the ethical validity of genetic databases, and their ultimate success, is the need to gain and maintain public trust in the enterprise. This can be achieved by a variety of means, including rigorous ethical scrutiny of the entire project, ensuring a high degree of openness and clear lines of accountability.

Existing databases should meet the requirements laid out in this report, to the extent that they relate to the maintenance and use of the database. The operation of all databases should be subject to regular, periodic ethical review.

Recommendation 5: Public debate should precede the establishment of new genetic databases. A database should not be established in the shadow of wide-spread public unease. Adequate mechanism to gain public trust must also be set in place. No database should be established if public trust is seriously in doubt.

Existing databases should meet the requirements laid out in this report, to the extent that they relate to the maintenance and use of the database. The operation of all databases should be subject to regular, periodic ethical review.

4. Informed Consent

4.1 Obtaining informed consent

The ethical principle of respect for autonomy requires that all research subjects give valid and informed consent before participating in any research study. There is no obvious reason to depart from this principle in the first instance when creating genetic databases. Therefore, those who provide samples or information for inclusion should do so on the basis of informed consent to participation. This is true irrespective of the uses to which the samples or the information might be put. Whatever is proposed should be consented to.

Recommendation 6: When obtaining informed consent to the provision of a sample or information for a genetic database, participants should be informed to the following extent:

(1) Participants should be given sufficient information to make a meaningful choice about participation in research leading to the establishment of a database, including information about the purposes of the database and its commercial potential;
(2) Sufficient information should be provided to ensure that participants comprehend the nature of the enterprise to their own satisfaction;
(3) Participants should be given the opportunity to ask questions and have these answered;
(4) Participants should be informed of the risks of participating, where these exist;
(5) Participants should be informed of the security provisions that exist to protect their personal data;
(6) Participants should be informed of the alternatives to participating, and in particular, should receive assurances that no adverse consequences will follow if they choose not to participate;
(7) Participants should be informed of the uses to which data might be put, including potential use to avoid harm to third parties, such as blood relatives;
(8) Participants should be informed of the possibility of future uses of data, beyond the limits of the present consent, and should be provided with an opportunity to withhold consent to such uses.

4.2 Anonymisation

Anonymisation of data or samples can go far in protecting the interests of the persons to whom they relate. Moreover, the use of anonymisation techniques can prescribe variable ethical response to the gathering and use of samples or data, since the risk of harm through misuse of

those samples or information is greatly reduced. When anonymisation occurs, the quality of the unique relationship that individuals have with their sample or their information is reduced, and this permits other interests to weigh more heavily in the balance. At no point, however, does that relationship cease to exist, for anonymisation is merely a process to ensure security of samples or data. Because no process is infallible, there always remains the possibility that anonymity can be breached and that significant harm to individuals will occur as a result. The fundamental interest that individuals have in their samples and/or genetic information must never be forgotten.

Two forms of anonymity exist. *Absolute anonymity* is achieved when no means are available to link data to an identifiable individual. *Proportional* or *reasonable anonymity* exists when no reasonable means of identification of specific individuals is available. In this latter respect, the use of linked or linkable coded information is a common means to achieve anonymity, when access to the link is restricted appropriately. In keeping with international standards of anonymisation, as laid down, inter alia, in the EC Directive on the Protection of Individuals with Regard to the Processing of Personal Data and on the Free Movement of Such Data, it is acceptable that proportional anonymity be used to secure genetic samples or genetic data, depending on how this is done, who is to have access and the uses which have been consented to. However, as a less secure method of protection, anonymisation alone does not necessarily meet the ethical requirements of respect for individuals. That is, mere compliance with legal standards of anonymity may not be enough, if, for example, anonymisation procedures are inadequate, without review, or otherwise defective in their protection of individual interests.

Recommendation 7: While the use of anonymisation can lead to a re-assessment of the balance between the protection of individual interests on the one hand, and the legitimate pursuit of public interests on the other, it is recommended that any anonymisation process be overseen by an independent body that would have the following obligations:
(1) To scrutinise and ensure the legitimacy of requests to the database;
(2) To act, where possible, as an intermediary between the creators and the users of the database, in respect of decoding apparatus used to anonymise and/or link data held on the database;
(3) To maintain standards and keep anonymisation processes under review.

4.3 The scope of consent

The starting point to determine the scope of valid consent is to ensure that specific consent is obtained for the specific purposes for which samples or information are taken. As part of this consent, participants should be informed of the likely risks and consequences. However, because by definition research involves matters of unknown future import, sometimes unexpected findings can be generated, and it is unclear what should be done with such results. Normally, research leads to abstract benefits, but if an immediate and clear benefit to identifiable individuals can be achieved, and if this will avert or minimise significant harm to the relevant individuals, then it may be legitimate to use research results to this end. In the context of genetics, this can mean the blood relatives of the person who has provided the original data. In such circumstances, the balance of harms may mean that it is permissible to inform third parties, even despite the wishes of the person who provided the original data. This course of action must, however, be justified by those who would undertake it, and ideally ethical approval should be sought, e.g. from the Ethical Approval Committee.

Recommendation 8: While, normally, genetic research data will remain of abstract significance, in limited circumstances data may be of value in a clinical setting. This use of data is permissible when:

(a) the data have been instrumental in identifying a clear clinical benefit to identifiable individuals;
(b) the disclosure of the data to the relevant individuals will avert or minimise significant harm to those individuals;
(c) there is no indication that the individuals in question would prefer not to know.
Disclosure in these circumstances is permissible even in the face of objection from the person who originally contributed data to the database. The onus is on those who would seek to disclose to justify this action. Ethical approval for such disclosures should be sought.

In some cases it might be desirable to seek broad, open-ended consent to future research, the purposes, limits or consequences of which are currently unknown. In such cases, blanket future consent is only permissible where anonymity can be guaranteed, and there is no risk that unexpected results will filter back to the subjects concerned. If this guarantee is not possible, or if linking of data is necessary for the research, then specific consent to the specific research must be obtained. The use of sunset clauses, whereby consent will only be valid during a finite period of time, might be considered as a means to ensure adequate protection of individual interests.

Recommendation 9: Blanket consent for future research is only permissible in circumstances where anonymity of future data can be guaranteed.

4.4 Research using archival material

Particular problems can arise over the use of archival material for genetic research purposes. Inter alia, these include the problem of obtaining valid and informed consent to such research. For example, it is possible for samples or information to have been given for one purpose in the past, and it is no longer possible or feasible to trace the sample source to gain consent to current proposed research. If it is proposed that research be done which might have direct significance to the individuals in question and they will be identifiable, then this research is only permissible if specific consent is obtained. To do otherwise would interfere too greatly with individual interests. It raises the spectre of causing considerable harm to individuals who are faced with a unwarranted approach with information that they might not wish to know. However, a more equal balance of interests can be achieved if samples and information are anonymised and there is a guarantee that no approach will be made to individuals in the future.

Recommendation 10: Research using archival material, such as pre-existing health records, specific health disorder databases or physical samples that have been retained - for which no specific consent has been obtained - is only permissible if the material and information derived from it is anonymised, and there is no prospect that research results will be used to identify the sample sources at any future time.

4.5 Using genetic material from vulnerable groups

The use of samples or information from vulnerable groups, such as children or incapacitated adults, must be subject to the same internationally agreed guidelines for research as embodied in instruments such as the Council for the International Organizations of Medical Sciences, International Ethical Guidelines for Biomedical Research Involving Human Subjects (1993) and the Declaration of Helsinki (2000). These instruments prescribe the utmost respect for research subjects, and require substituted consent from a guardian of the incapax individual. At all times, the risks must be minimal. These provisions apply equally in the present context.

Recommendation 11: Research using samples or genetic information taken from vulnerable subjects, such as incapacitated adults or children, must be carried out in full conformity with internationally agreed principles and guidelines. Research must be shown to hold the reasonable prospect of benefiting the class of persons to which the particular subject belongs, either in the immediate or the foreseeable future.

The generation of genetic data using samples taken from minors is particularly sensitive, because this can reveal information about a child's future health which can impact profoundly on their childhood. Evidence exists, for example, of children being treated by parents as though they have a disease, when all that genetic information has revealed is a predisposition to disease, or an indication that disease might occur at some future date, for example, in adult years. The generation of this information therefore potentially impacts greatly on a child's life, and it is permissible only in clearly defined circumstances.

Recommendation 12: The taking of samples or generation of genetic information for research purposes must respect the child's confidentiality and must only be undertaken with the explicit approval of a competent research ethics committee. It is acknowledged that some research will require the linking of clinical and genetic data in order to proceed and that the main beneficiaries of this research may be future children rather than the child who provides the sample. In such cases data should be coded to prevent identifiable links being made with access to the key to the code being restricted and subject to separate permission on each occasion. Such permission would only normally be granted in the event of a direct clinical benefit to the child. Where a child is able to consent or refuse to participate this must be respected.

4.6 Using material from deceased persons

The death of an individual who has provided a genetic sample of genetic information does not represent the end of the ethical responsibilities that are owed in respect of the sample or information. Death only affects the primacy of the interests of the sample source, and does not extinguish them. The scientific interest in the data remains. Moreover, the interests of blood relatives, where these are strong, also remain. This includes the interests of future blood relatives. Thus security of samples and data must remain in force. It may, nevertheless, be legitimate to revisit the balance of interests and readjust these accordingly. In such cases, appropriate ethical approval should be sought for any change of use of genetic samples or data.

Recommendation 13: Death of a sample source only affects the primacy of his/her interests, it does not extinguish them. Other interests, such as those of researchers or family members (including future family members) remain valid. If it is thought appropriate to readjust the balance of interests in light of death, then appropriate ethical approval should be sought to do so.

4.7 Departing from the practice of prior informed consent

The principle of respect for autonomy and the doctrine of informed consent prescribe that consent should be obtained from sample sources before any research is undertaken. However, this is not an approach of universal application, and exceptions can be justified in rare circumstances.

It is a fundamental premise of this report that a balance of interests should be considered in the context of genetic databases. In this, sight should never be lost of the fact that respect must be due to individuals at all times, and they should be protected from harm where possible.

However, these imperatives need not be met in any prescribed way. That is, respect and protection from harm can be assured by a variety of means. This raises the question of whether informed consent may be eschewed in the interests of a greater public good. In particular, is it acceptable to proceed with genetic research and the creation of a genetic database with pre-existing information, even when consent has not been sought or obtained?

Autonomy and informed consent would indicate that individuals should be at liberty to choose whether to opt-in to any proposed research. This can, however, be problematic in research terms because the requirement to obtain consent from a large population might be infeasible, and there is the risk that insufficient number of persons will come forward, undermining the value of any research that can be carried out. An alternative is to assume that the population in question consents unless individual members of that population indicate otherwise, that is, opt-out. This is a controversial proposal, and requires justification in the strongest possible terms.

Recommendation 14: Those who would seek to depart from the practice of requiring active informed consent prior to participation in the creation of a genetic database must justify this position in strong ethical terms. As a minimum the following criteria must be satisfied: (a) a clear, realisable and significant public health benefit must be identified, (b) the widest possible educational programme must be instituted among the population that will participate, including an opportunity for public debate (c) strong privacy protection measures must be implemented, (d) individuals must at all times be given the opportunity to refuse to participate, and (e) every stage of the process must be subject to the most stringent ethical scrutiny.

5. Privacy Protection

5.1 The importance of adequate privacy protection

Various methods of collection generate various types of genetic information. The paradigm example is direct analysis of DNA, but other means are possible, including direct observation of individuals. However, the power of genetic information lies in its ability to inform and influence an individual's circumstances. The greater the impact that use or misuse of the information might have, the greater the sensitivity it carries, and so the greater the need for its protection. It is primarily because of the significant harm that misuse of information can cause individuals that privacy is so dearly held. While this is true of all forms of personal information, some forms of genetic information are particularly sensitive, and so in particular need of protection.

5.2 Storage of genetic samples and genetic information

The onus of ensuring adequate protection of privacy falls on the shoulders of those who gather and use genetic information and samples, especially if this is with a view to storage in a database. The adequacy of privacy protection measures must be examined and subjected to ethical scrutiny, for example by the Ethical Approval Committee, and all methods of storage must be linked to the function and purpose of the database. Moreover, these must be in line with existing legal protections, as embodied, inter alia, in data protection laws. At all times, transparency of procedures and methods must be maintained.

Recommendation 15: The gathering and storage of genetic samples and information must be subject to rigorous privacy protection measures and in conformity with international and

national data protection laws. These privacy measures must be transparent and subject to ethical approval by a suitable body.

5.3 The right not to know

The principle of respect for autonomy requires that individual choices not only be respected, but that they also be informed. In order for choices to be informed individuals need knowledge. Yet, it is an unfortunate result of the modern imperative to respect autonomy that often it is presumed that to inform is necessarily to respect the individual. But this is not necessarily true in circumstances where one has no indication that an individual would wish to know. Indeed, unsolicited genetic information can be harmful to individuals, especially in circumstances when it reveals the likelihood of the onset of disease when there is no available therapy or cure. Thus, in the search for an ethically acceptable balance of interests, it is important also to weigh in the balance the possible interest that individuals might have in not knowing information.

Unfortunately, in circumstances where there is no evidence of what an individual would want to know, it is not possible to seek to advance their autonomy by asking them if they would wish to know, for to do so is to indicate that there is, indeed, something to know, and thereby any possible harm will have been caused. Rather, the right not to know is a form of privacy interest that can be respected and protected by ensuring that due regard is paid to the state of separateness enjoyed by individuals as an aspect of their individuality. It is a state that cannot be entered without due cause and good reason. A weighing of a relevant set of factors should be undertaken in deciding if disclosure is warranted.

Recommendation 16: Adequate account must be taken of the privacy interest that individuals have in not knowing information about themselves. Before any unsolicited approach is made, the following factors must be considered:

(1) the availability of a cure or therapy;
(2) the severity of the condition and likelihood of onset;
(3) the nature of the genetic disease;
(4) the genetic nature of the disease, i.e. - that it might have significant implications for blood relatives;
(5) the nature of any genetic testing that will be required;
(6) the question of how the individual might be affected if subjected to unwarranted information, and whether the individual has expressed any views on receiving information of this kind.

6. Rights of Access and Control

6.1 Regulating access to genetic databases

Access to a genetic database might be sought by a number of interested parties. Access provisions should be linked to the legitimate purposes of the database and subject, in the first instance, to the consent of participants. This principle may only be departed from if data have been adequately anonymised. Access to data by parties primarily concerned with their own financial interests, such as insurers or employers, should not normally be permitted.

Different requirements will apply depending on whether genetic samples or genetic information are to be accessed. While the later is intangible and therefore potentially an inexhaustible

resource, the former is a finite resource, and responsible and judicious use of samples is therefore required. Any such uses should also be subject to ethical approval.

Recommendation 17: It should be the role of an independent body to oversee and regulate access to genetic databases. This same body should hold the key to any anonymisation methods that have been used. The body should receive applications for access, and these should be considered in light of the nature and purposes of the database. Moreover, the body must be satisfied that the party seeking access is able to make responsible use of the data and to continue to respect their status. The use of finite resources such as genetic samples must equally be regulated by ethically appropriate means.

6.2 Subject Access and Withdrawal Rights

Where personally identifiable information is held in a database, then subject access rights to this information should be granted. These rights should be akin to those embodied in international data protection instruments, such as the *EC Directive on the Protection of Individuals with Regard to the Processing of Personal Data and on the Free Movement of Such Data.*

Where personally identifiable information remains in a database or where personally identifiable samples are held, then so long as it is reasonably practicable, the individual to whom the information or sample relates, is entitled to request removal of the information from the database at any time, and/or destruction of the sample. This provision is unwaiverable by consent, except where absolute anonymity is guaranteed. In other cases the onus is on the holder of the information or sample to show that it is not reasonably practicable to comply with this request.

Recommendation 18: Personally identifiable information held on a database should be subject to adequate subject access rights, in line with existing international measures. This information, and any personally identifiable samples also held, should be destroyed on the request of the subject. This provision is not waiverable by consent, except where absolute anonymity is guaranteed. In other cases, this request must be complied with unless the holder of the information or the sample can show that it is not reasonably practicable to do so.

Access to anonymised data by the data subject, by definition, is not possible. However, this in no way detracts from the obligation of the data holder to ensure adequate anonymisation and privacy protection measures.

7. Economic Interests

7.1 Recognising individual interests

Individuals have an interest in their genetic samples and genetic information that is akin to a property right. There is strong normative appeal in applying a property model to make sense of the relationship between an individual and her samples or genetic information. Property is one of the most effective and respected means of exercising control in contemporary society, even if it does not confer absolute rights of control. This having been said, the property model does not fit easily when applied to human material or genetic information. Thus, it is acknowledged that there might be hurdles to embodying this interest in legal property rights. None the less, there is

no objection in principle to allowing individuals to engage in the commercial process, subject to adequate protection from exploitation or undue harm.

The recognition of the potential value of human material or human genetic information should be accompanied by due recognition of the inherent value of the persons from whom this material or information is derived. While there is no right to demand a benefit in clinical terms from the existence or operation of a genetic database, the emphasis should be placed on the legitimate and strong interest that participants have in receiving an ultimate return from the research, either qua individual, or qua member of the general class of persons who might ultimately enjoy benefit, such as those affected by the disease that is the subject of the research. This interest could be strengthened if the surrender of research material were possible on the basis of an undertaking to provide some sort of return in kind. This is particularly true when a group benefit could be realised, this being perhaps the most equitable return.

Recommendation 19: Serious consideration should be given to recognising property rights for individuals in their own body samples and genetic information derived from those samples. In all circumstances, the provision of research materials, including DNA samples, should be on the undertaking that some kind of benefit will ultimately be returned, either to the individual from who the materials were taken, or to the general class of person to which that individual belongs.

7.2 Public/Private Partnerships

Partnership between public and private enterprises would currently seem to be the optimal means to realise public benefit from research in genetics. Accordingly, such partnership is not unacceptable in se. Indeed, the means by which funding for research is provided should be less of a concern than ensuring that adequate safeguards are instituted to ensure that the public benefit of the research is realised, and that the research is carried out in a manner that is ethically justifiable. Thus, whether funding comes from a public, private or voluntary source, all research should be subject to the same ethical scrutiny.

7.3 Intellectual Property Rights

A number of intellectual property rights may be granted to researchers or those who create and manage genetic databases. Patent rights are available for inventions using human material, and both copyright and database rights can be claimed in respect of the structure, content, selection and arrangement of a database.

It is important to understand that such rights do not accord an unfettered reign to the rights holders to do what they wish with their property. Indeed, the very nature of the intellectual property system reflects the balance of interests that this report promotes. Moreover, intellectual property rights in the products of research can ensure both private and public interests, at least in theory. And, if at times the practice departs from this, the obligation must be to seek a more equitable equilibrium in the relative weighing of interests.

8. Accountability and Transparency

8.1 Achieving transparency

It is crucial to the achievement of public trust and confidence in genetic databases that as much transparency be achieved as possible. Public debate prior to the establishment of the database should serve to heighten awareness and foster trust in the endeavour, and participants should be well informed about their involvement. Throughout its existence a database should be subject to openness and review by an appropriate ethical body, and this should be tailored to reflect the nature and content of particular databases.

Recommendation 20: The establishment, maintenance and operation of genetic databases should be carried out in an atmosphere of openness, transparency and appropriate ethical scrutiny.

8.2 Protecting legitimate commercial confidentiality

Research databases invariably contain commercially sensitive information. It is acceptable for this information to be kept confidential to protect the commercial interests of the relevant parties, subject, however, to full disclosure of the nature of those interests and appropriate ethical review of the commercial interests that are furthered through the database. At no point is it acceptable to further commercial interests at the expense of the protection of the interests of the individuals who have contributed to the database or provided genetic samples. More consideration should be given to the precise circumstances in which commercially significant data may be kept confidential.

Recommendation 21: While it is accepted that in certain cases commercially sensitive data derived from a database can be kept confidential, more consideration is required of the precise circumstances in which this will be permissible. It will never be permissible if this would seriously prejudice the interests of individuals who have contributed samples or information to the database.

8.3. Ensuring Accountability

Accountability of database creators, managers and users should be a given. Consideration should be made of the ways in which this can be achieved, including legal measures to regulate and control the creation and management of databases. One model is the establishment of a regulatory body with a power to grant licences to create and operate databases. No database would be legal without the appropriate licence. This body might also oversee and monitor the process and outcome of research activities involving genetic databases. Such a body could either be the Ethical Approval Committee outlined above, or a modified form of the Data Protection Commission which many jurisdictions have established to monitor data protection laws.

Recommendation 22: Accountability of database creators, managers and users should be a given. Consideration should be made of the ways in which this can be achieved, including legal measures to regulate and control the creation and management of databases, and duties to report publicly on activities in respect of the database.

Summary of Recommendations

Recommendation 1: The World Health Organisation should investigate the issues raised by genetic databases from perspectives other than that which reflects a western, Judeo-Christian ethic.

Recommendation 2: The intimate and unique relationship that individuals have with body samples or information derived from them deserves full recognition and proper respect. Individuals are entitled to control over the use of their samples and information, in a manner akin to a property right. This right may, however, be subject to waiver or certain limits, such as when anonymisation occurs (and so the relationship is lost), or when certain uses may cause harm to others.

Recommendation 3: The collection of genetic data should be only be allowed, in the first instance, for the purpose of promoting public health. The onus is on those who would seek to use data outside this purposes to justify doing so.

Whatever the reasons for the establishment of a genetic database, the onus will be on those who seek to create the database to justify its nature, purposes, content and uses. In particular the following factors must be satisfactorily established:

(1) The public interest that will be furthered by the creation of the database;
(2) The relevance of genetic data to the purposes of the database;
(3) That the creators of the database are able to restrict the use of the data to the purposes for which it was sought;
(4) That the creators of the database are able to ensure adequate security measures for the data and for privacy protection;
(5) That the creators and users of the database have sufficient competence to understand the data;
(6) That the creators and users of the database have the ability to understand the context in which the information comes, and the relevance of other factors which further contextualise the information.
(7) That the creators have considered ethical aspects and made appropriate provisions to respect human rights.

Recommendation 4: It is recommended that an appropriate ethical approval mechanisms be established to oversee the creation and maintenance of genetic databases. An appropriate means to do so would be to establish an Ethical Approval Committee with the following duties:

(1) To ensure minimal standards and public trust in the database;
(2) To scrutinize the scientific validity of any proposal to establish a database;
(3) To ensure the reputation and integrity of the creators of the database;
(4) To verify that an identified public interest can be furthered by the establishment of the database;
(5) To assess and review the adequacy of security provisions of the data held on the database for the protection of privacy;
(6) To assess and review any other proposed protection mechanisms in respect of the persons to whom the data relate;

(7) To consider and address ethical questions concerning the use of the database, and the data contained therein;
(8) To produce Codes of Conduct governing the establishment and maintenance of genetic databases.

It should be borne in mind that such an ethical body would require to reflect the particular context in which genetic data were being generated and used. In particular, the composition of the body, and its focus, will be different depending on whether the genetic data exist in the context of (a) pure research, (b) clinical research, or (c) clinical practice.

Recommendation 5: Public debate should precede the establishment of new genetic databases. A database should not be established in the shadow of wide-spread public unease. Adequate mechanism to gain public trust must also be set in place. No database should be established if public trust is seriously in doubt.
Existing databases should meet the requirements laid out in this report, to the extent that they relate to the maintenance and use of the database. The operation of all databases should be subject to regular, periodic ethical review.

Recommendation 6: When obtaining informed consent to the provision of a sample or information for a genetic database, participants should be informed to the following extent:

(1) Participants should be given sufficient information to make a meaningful choice about participation in research leading to the establishment of a database, including information about the purposes of the database and its commercial potential;
(2) Sufficient information should be provided to ensure that participants comprehend the nature of the enterprise to their own satisfaction;
(3) Participants should be given the opportunity to ask questions and have these answered;
(4) Participants should be informed of the risks of participating, where these exist;
(5) Participants should be informed of the security provisions that exist to protect their personal data;
(6) Participants should be informed of the alternatives to participating, and in particular, should receive assurances that no adverse consequences will follow if they choose not to participate;
(7) Participants should be informed of the uses to which data might be put, including potential use to avoid harm to third parties, such as blood relatives;
(8) Participants should be informed of the possibility of future uses of data, beyond the limits of the present consent, and should be provided with an opportunity to withhold consent to such uses.

Recommendation 7: While the use of anonymisation can lead to a re-assessment of the balance between the protection of individual interests on the one hand, and the legitimate pursuit of public interests on the other, it is recommended that any anonymisation process be overseen by an independent body that would have the following obligations:
(1) To scrutinise and ensure the legitimacy of requests to the database;
(2) To act, where possible, as an intermediary between the creators and the users of the database, in respect of decoding apparatus used to anonymise and/or link data held on the database;
(3) To maintain standards and keep anonymisation processes under review.

Recommendation 8: While, normally, genetic research data will remain of abstract significance, in limited circumstances data may be of value in a clinical setting. This use of data is permissible when:

(a) the data have been instrumental in identifying a clear clinical benefit to identifiable individuals;
(b) the disclosure of the data to the relevant individuals will avert or minimise significant harm to those individuals;
(c) there is no indication that the individuals in question would prefer not to know.
Disclosure in these circumstances is permissible even in the face of objection from the person who originally contributed data to the database. The onus is on those who would seek to disclose to justify this action. Ethical approval for such disclosures should be sought.

Recommendation 9: Blanket consent for future research is only permissible in circumstances where anonymity of future data can be guaranteed.

Recommendation 10: Research using archival material, such as pre-existing health records, specific health disorder databases or physical samples that have been retained - for which no specific consent has been obtained - is only permissible if the material and information derived from it is anonymised, and there is no prospect that research results will be used to identify the sample sources at any future time.

Recommendation 11: Research using samples or genetic information taken from vulnerable subjects, such as incapacitated adults or children, must be carried out in full conformity with internationally agreed principles and guidelines. Research must be shown to hold the reasonable prospect of benefiting the class of persons to which the particular subject belongs, either in the immediate or the foreseeable future.

Recommendation 12: The taking of samples or generation of genetic information for research purposes must respect the child's confidentiality and must only be undertaken with the explicit approval of a competent research ethics committee. It is acknowledged that some research will require the linking of clinical and genetic data in order to proceed and that the main beneficiaries of this research may be future children rather than the child who provides the sample. In such cases data should be coded to prevent identifiable links being made with access to the key to the code being restricted and subject to separate permission on each occasion. Such permission would only normally be granted in the event of a direct clinical benefit to the child. Where a child is able to consent or refuse to participate this must be respected.

Recommendation 13: Death of a sample source only affects the primacy of his/her interests, it does not extinguish them. Other interests, such as those of researchers or family members (including future family members) remain valid. If it is thought appropriate to readjust the balance of interests in light of death, then appropriate ethical approval should be sought to do so.

Recommendation 14: Those who would seek to depart from the practice of requiring active informed consent prior to participation in the creation of a genetic database must justify this position in strong ethical terms. As a minimum the following criteria must be satisfied: (a) a clear, realisable and significant public health benefit must be identified, (b) the widest possible educational programme must be instituted among the population that will participate, including an opportunity for public debate (c) strong privacy protection measures must be implemented, (d) individuals must at all times be given the opportunity to refuse to participate, and (e) every stage of the process must be subject to the most stringent ethical scrutiny.

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